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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/544,115	08/01/2005	Marius Clore	3514.160B-US	5005

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EXAMINER	
AUDET, MAURY A	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/544,115	CLORE ET AL.	
	Examiner	Art Unit	
	MAURY AUDET	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *18-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-17* is/are rejected.

7)☒ Claim(s) *1-17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *8/1/05* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/3/06, 8/16/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-17, as drawn to the elected peptide invention SEQ ID NO: 3, in the reply filed on 11/2/07, is acknowledged. Claims 18-20 are withdrawn as being drawn to non-elected subject matter.

Claim Objections

Claims 1-17 are objected to because of the following informalities: the claims have not been amended to the elected peptide invention of the 36-mer HIV variant, SEQ ID NO: 3 (invention not species). As the peptide was not found to be reasonably taught or suggested by the prior art of record, the claims would likely receive favorable consideration if amended thereto, notwithstanding the other outstanding rejections.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-17 are rejected under 35 U.S.C. 102(a) as being anticipated by Bewley et al. (J. Biol. Chem. 2002 Apr 19;277(16):14238-45. Epub 2002 Feb 21). Published 10 dates before the 1-year anniversary of Applicant's earliest effective priority date, 2 of 4 authors listed constitute 2

of the 3 listed present inventors in this application. Based on the latter, it unclear who invented what or should constitute an inventor of SEQ ID NO: 3? [The Examiner is a little confused as to how this reference was not cited in either of the Information Disclosure Statements?].

Bewley et al. teach SEQ ID NO: 3 as one of the peptides below:

The pre-hairpin intermediate of gp41 from the human immunodeficiency virus (HIV) is the target for two classes of fusion inhibitors that bind to the C-terminal region or the trimeric coiled-coil of N-terminal helices, thereby preventing formation of the fusogenic trimer of hairpins. Using rational design, two 36-residue peptides, N36(Mut(e,g)) and N36(Mut(a,d)), were derived from the parent N36 peptide comprising the N-terminal helix of the gp41 ectodomain (residues 546-581 of HIV-1 envelope), characterized by analytical ultracentrifugation and CD, and assessed for their ability to inhibit HIV fusion using a quantitative vaccinia virus-based fusion assay. N36(Mut(e,g)) contains nine amino acid substitutions designed to disrupt interactions with the C-terminal region of gp41 while preserving contacts governing the formation of the trimeric coiled-coil. N36(Mut(a,d)) contains nine substitutions designed to block formation of the trimeric coiled-coil but retains residues that interact with the C-terminal region of gp41. N36(Mut(a,d)) is monomeric, is largely random coil, does not interact with the C34 peptide derived from the C-terminal region of gp41 (residues 628-661), and does not inhibit fusion. The trimeric coiled-coil structure is therefore a prerequisite for interaction with the C-terminal region of gp41. N36(Mut(e,g)) forms a monodisperse, helical trimer in solution, does not interact with C34, and yet inhibits fusion about 50-fold more effectively than the parent N36 peptide (IC(50) approximately 308 nm versus approximately 16 microm). These results indicate that N36(Mut(e,g)) acts by disrupting the homotrimeric coiled-coil of N-terminal helices in the pre-hairpin intermediate to form heterotrimers. Thus N36(Mut(e,g)) represents a novel third class of gp41-targeted HIV fusion inhibitor. A quantitative model describing the interaction of N36(Mut(e,g)) with the pre-hairpin intermediate is presented.

35 U.S.C. 112, 1st Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

> The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The instant disclosure fails to meet the enablement requirement for SEQ ID NO: 3 of pharmaceutically able to inhibit the fusion of HIV-1 to a human cell.

fragments, for the following reasons:

The nature of the invention: The claimed invention is drawn to a peptide of SEQ ID NO: 3 and "pharmaceutical" application whereby said peptide inhibits fusion of HIV-1 to a human cell. In other words, to function as a vaccine.

The state of the art:

Bewley et al. (J. Biol. Chem. 2002 Apr 19;277(16):14238-45. Epub 2002 Feb 21) discussed above teach that SEQ ID NO: 3 is as an "N36(Mut(e,g)) represents a novel third class of gp41-targeted HIV fusion inhibitor" (abstract).

However, Ray et al. (J Virol. 2007 Apr;81(7):3240-50. Epub 2007 Jan 24) teach that with the evolution of the HIV-1 virus, even in the same patient, it is unclear what fusion inhibitors or other HIV-type inhibitors will even work from one patient to another (abstract):

> The clinical use of the human immunodeficiency virus (HIV) fusion inhibitor enfuvirtide (ENF) can select for drug-resistant HIV-1 strains bearing mutations in the HR1 region of the viral envelope (Env) protein. We analyzed the properties of multiple Env proteins isolated from five patients who experienced an initial decline in viral load after ENF therapy followed by subsequent rebound due to emergence of ENF-resistant HIV-1. Prior to ENF therapy, each patient harbored genetically and phenotypically diverse Env proteins that used CCR5 and/or CXCR4 to elicit membrane fusion. Coreceptor usage patterns of the Envs isolated from two patients underwent homogenization following ENF therapy, whereas in the other three patients, recombination appeared to allow the introduction of a single HR1 sequence with ENF resistance mutations into phenotypically distinct Env proteins. Analysis of individual Env clones also revealed that prior to ENF therapy, there was sometimes marked heterogeneity in the susceptibility of individual Env proteins to coreceptor inhibitors. After virologic failure, all Envs acquired resistance to ENF but exhibited no consistent change in their sensitivity to the fusion inhibitor T-1249 or to coreceptor inhibitors. In summary, using patient-derived Env proteins, we found that ENF failure was associated with emergence of high-level resistance to ENF due largely to mutations in HR1 but that susceptibility to other entry inhibitors was unaffected, that in these late-stage patients there was greater clonal variability to coreceptor than to fusion inhibitors, and that recombination events in vivo could sometimes restore Env genotypic and phenotypic heterogeneity by introducing drug-resistant gp41 sequences into heterologous gp120 backgrounds.

Thus, with an evolving virus, even within the same patient, it is unclear how any asserted "HIV fusion inhibitor" can so-be classified?

The amount of direction or guidance present and the presence or absence of working examples: Enablement must be provided by the specification unless it is well known in the art.

In re Buchner 18 USPQ 2d 1331 (Fed. Cir. 1991). The specification describes that as engineered, SEQ ID NO: 3, is believed to be able to function as an HIV fusion inhibitor, inhibiting the fusion of HIV to human T cells. Example 1 discusses cell fusion assays, yet it was not found in this Example or any of the other 4 Examples, where SEQ ID NO: 3 was actually in fact tested for its ability to inhibit HIV fusion to human cell lines.

The breadth of the claims and the quantity of experimentation needed: Given the uncertainty as to whether even known HIV fusion inhibitors are capable of functioning *in vivo*, and the breadth of the claims thereto or pharmaceutical compositions thereof., absent sufficient teachings in the specification to overcome the teachings of unpredictability found in the art; it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAURY AUDET whose telephone number is (571)272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MA, 3/15/08

/Maury Audet/
Examiner, Art Unit 1654